Group VI: Claims 18, 19, 33-35 drawn to a method of treatment of donor tissues to reduce the risk of rejection further comprising treating the tissue with an agent to prevent tissue senescence or cell death;

Group VII: Claims 24 and 25 drawn to non-human mammalian donor tissues; and

Group VIII: Claims 26 and 27 drawn to a method of assessing tissue damage comprising detecting the accumulation of cytological markers of tissue stress.

Applicant respectfully traverses the restriction between the Groups I -VIII inventions. A withdrawal or modification of the restriction requirement is clearly in order for the reasons set forth below.

The restriction requirement set forth above is improper for failure to comply with the relevant provisions of the Manual of Patent Examining Procedure (M.P.E.P.) pertaining to unity of invention determinations.

The present application was filed under 35 U.S.C. §371 as a U.S. national stage application under the Patent Cooperation Treaty.

As stated in § 1893.03(d) of the M.P.E.P.:

> Examiners are reminded that unity of invention (not restriction) practice is applicable in international applications (both Chapter I and II) and in national stage applications submitted under 35 U.S.C. § 371...
>
> The principles of unity of invention are used to determine the types of claimed subject matter and the combinations of claims to different categories of invention that are permitted to be included in a single international or national stage patent application. The basic principle is that an application should relate to only one invention or, if there is more than one invention, that applicant would have a right to include in a single application only those inventions which are so linked as to form a single general inventive concept.
>
> A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention, considered

as a whole, makes over the prior art....

It is the Examiner's position that the inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1, because, under PCT Rule 13.2, they lack the same or corresponding special technical feature. The Examiner contends that the subject matter of claims 1-22, 24-25 is known from the disclosure in GB2321642 A. Applicants strenuously disagree with the Examiner in this regard and respectfully submit that the GB2321642 patent is silent regarding the use of a telomerase binding proteins in methods for screening donor tissues for predisposition to rejection. Accordingly, the requirement for restriction is in error and should be retracted.

The present application was filed under 35 U.S.C. §371 as a U.S. national stage application under the Patent Cooperation Treaty. The requirements of the PCT are, of course, supposed to take precedence over normal national practice for the national phase of a PCT application. In particular, it is not permissible under the PCT for national offices to require compliance with the requirements relating to the form or contents of the application different from or additional to those which are provided for in the PCT (Art 27 PCT). In this specific instance, the PCT Handbook says at section 33.35, paragraph 2 "a designated office ought not to raise an objection as to a lack of unity when the International Searching and/or Preliminary Examining Authority has found that the claims comply with the requirement for unity of invention". Indeed, the PCT Contracting States have agreed to this principle, according to the PCT Handbook at Section 23.9 paragraph 2 (which refers to the report of the PCT assembly, 18th session (1991), item 24).

Notably, during the international stage of this application, the Examiner **did not** make a lack of unity finding and considered all of the claims to be directed to a single

invention. Plainly, the written restriction requirement fails to comply with the established United States Patent and Trademark Office practice of following the international rules regarding unity of invention in the prosecution of applications filed under § 371. It is unclear how the Examiner could conclude that instant application now has eight Groups of inventions, when the international application from which it originates has unity of invention.

Finally, according to the MPEP §803.01, there are two criteria for restriction between inventions which are alleged to be patentably distinct: 1) the inventions must be independent and distinct as claimed and 2) there must be a serious burden on the Examiner if the restriction is not required.

As set forth above, the Examiner has asserted that the claims are directed to eight groups of patentably distinct inventions. Applicant strenuously disagrees. For example, Claim 1 reads on method for screening donor tissues for a predisposition to rejection by determining the expression level of **at least one** endogenous telomere binding protein. Claims 5 and 6 depend directly or indirectly from claim 1. Accordingly, the subject matter of claims 5 and 6 which comprise separate groups of invention cannot be considered "independent" of the Group I invention. Inasmuch as claim 1 reads on "at least one", the methods of claims 5 (Group II) and 6 (Group III) which specify determining the expression levels at least two or three telomerase binding proteins respectively, cannot reasonably be considered patentably distinct from the method of the Group I invention.

Applicants respectfully submit that the Examiner's workload would not be increased by searching the invention of the Groups I, II and III inventions as presently claimed and request that at a minimum, the restriction between these Groups be withdrawn. Clearly, a proper search of the subject matter of the Group I invention would encompass the subject

matter of claims 5, 30, and 6 thus would not unduly increase the Examiner's search burden.

Applicants also strenuously traverse the Examiner's requirement that a single protein in the Markush groups of the claims be elected as a single invention. Clearly, this requirement is onerous as Applicants would be forced to file 33 applications to protect each member of the Markush group disclosed. As set forth in the MPEP at §803.02, if the members of the Markush group are sufficiently few in number, or closely related (e.g., indicative of a predisposition to rejection) such that a search of the claim can be performed without undue burden, the Examiner must examine all members of the Markush group in the claim on the merits even if they are directed to separate and distinct inventions. Applicants respectfully submit that a requirement for an election of species rather than an invention election, would be more appropriate in this case and in keeping with the provisions of the MPEP.

In order to be fully responsive however, Applicants hereby elect the claims of the Group I invention for prosecution at this time. Applicants also elect G22P1 as the telomere binding protein. All of the pending claims read on the elected species.

Applicants reserve the right to file one or more continuing applications under 35 U.S.C. §120 on the subject matter of any claims finally held withdrawn from consideration in this application.

Favorable consideration leading to prompt allowance of the present application is respectfully requested.

Respectfully submitted,
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